REMARKS

With the entry of the present amendment, claims 16-20, 23-42 and 50-56 are in this application. Claims 1-15, 21-22 and 43-49 have been canceled without prejudice. The format of claim 16 has been changed to conserve space and to add commas, but the content, but for dependency which is amended to reflect replacement of claim 1 with claim 56. Claim 23 has been amended to refer only to provision of refugia, in view of the amendment to the base claim. New claims 50-52 have been presented; support is found on page 12, lines 6 and 10 (female specific is implicit basis for either sex and there are numerous other references to sex-specificity in the description). New US claims 53 and 54-55 have presented; claim 53 more closely defines the pesticide of claim 1 as being "a chemical pesticide." Support is found at page 7, line 28 of the as-filed specification and in the second paragraph on page 9. New claim 54 specifies that the "first trait confers resistance to a pesticide or tolerance to predators, viruses, parasites or parasitoids". This allows for means such as predators (as well as viruses, parasites or parasitoids) that can also be used to control the target insect population; support is found at page 7, lines 27 to 31, of the as-filed specification. Claim 55 is supported by claim 34. New claim 56 presents subject matter supported by as-filed claims 1, 2, 14, 15, 22 and 23 and in the as-filed Specification at page 9, line 13, and page 11, second paragraph. Claims previously depending from claim 1 have been rewritten to depend from new claim 56. Dependent claims have been amended to begin with "the" rather than "a". None of the amendments made herein constitutes the addition of new matter.

The Objections to the Claims

The Patent Office has objected to claim 2, alleging that the use of non wild type or wild type counterpart is confusing.

Claim 2 has been canceled without prejudice in the present amendment, thus rendering this objection moot.

Claim 21 has been objected to as being of improper dependent form for failing to limit the subject matter of a previous claim.

Claim 21 has been canceled without prejudice in the present amendment, thus rendering this objection moot.

Claims 37 and 44 have been objected to for lack of periods at the ends.

In the interest of advancing prosecution, Applicants have amended claim 37 to add the necessary punctuation. Claim 44 has been canceled without prejudice in the present amendment, thus rendering this objection moot.

The Rejections under 35 U.S.C. 112, paragraph

Claims 1, 2, 14, 19-24 and 26-49 have been rejected as allegedly lacking enablement of a method of inhibiting the spread of a non-wild-type trait in organisms other than insects. Applicants respectfully traverse this rejection.

The Patent Office has acknowledged that the Specification is enabling for a method of inhibiting the spread of a non-wild-type trait in insect pests by introducing sexually compatible individuals substantially homozygous for a conditional dominant lethal gene counterpart to the wild-type trait in insect pest populations.

In the interest of advancing prosecution and without acquiescing to the rejection, Applicants have replaced claim 1 with new claim 56, which is related to the genes and counterparts as shown in the Specification. The claims have been amended to insects in combination with the negative effects exerted by certain insect control agents on a target insect population. These control agents can be a pesticide(claims 1-53) or a pesticide as well as predators, viruses, parasites or parasitoids (claim 54). All these agents set out to limit or eradicate the first trait. All that the invention requires is that the first trait confers an advantage on the pest population. This advantage is the ability to avoid the normal methods of controlling said population. These methods of control may be the use of a pesticide or a predator etc: both are capable of, and are generally used to, control (i.e. weaken or exert a negative effect on the) insect pest populations.

In the interest of advancing prosecution and without acquiescing to the rejection, Applicants have amended the claims to recite a target insect population.

Applicants respectfully maintain that the invention as claimed is adequately enabled so as to allow one of ordinary skill in the art to practice the presently claimed invention without the expense of undue experimentation. It is believed that this renders the rejection moot and the withdrawal of the rejection is respectfully requested.

The Rejections under 35 U.S.C. 102

Claims 1, 2, 14-21, 31 and 33-49 have been rejected as allegedly lacking novelty over Alphey (WO 01/39599). Applicants respectfully traverse this rejection.

The cited reference is said to anticipate the method of inhibiting the spread of wild-type genes in insects by distributing insects homozygous at more than one locus expressing conditionally suppressible dominant lethal non-wild-type counterpart genes selective for females.

The Examiner has acknowledged the novelty of claim 22 (use of pesticides) over the earlier publication (Alphey *et al*) of the RIDL method by the present inventor and disclosed in the present application. In other words, Alphey teaches the use of dominant lethal genes in methods of population control. However, there is not a single mention of pesticides in the cited Alphey reference. The only mentions made of toxins therein are in respect of the lethal genes themselves, not an outside factor against which resistance may be overcome, as in the present claims. The same applies to the (pesticides or) predators, etc. in claim 54. There is also absolutely no disclosure of releasing substantially homozygous wild type individuals sensitive to a pesticide. Furthermore, there is also no disclosure of treating with pesticides or using refugia. Thus, the claims are novel over Alphey on several points.

In view of the foregoing arguments, the cited reference does not anticipate the present claimed invention, and Applicants respectfully request the withdrawal of the rejection.

The Rejections under 35 U.S.C. 103

Claims 27-30 have been rejected as allegedly unpatentable over Alphey (WO 01/39599). Applicants respectfully traverse this rejection.

Alphey is said to lack teachings of the specific calculations for determining optimal quantities of genetically engineered insects introduced into a target population, but Alphey is said to discuss introducing a genetically engineered adults at a single point in time or introducing a normal population of genetically engineered individuals to prolong exposure to the wild-type population. The Patent Office has concluded that it would have been obvious at the time the invention was made to release a specific percentage of recombinant individuals to reduce a wild-type trait or genes.

It will be appreciated that the present invention seeks to limit the spread, within an insect population, of certain traits. These traits, once they have spread throughout the population, would essentially otherwise prevent the user from controlling these pests. One way to control the pest population in an area is to expose that area to a pesticide. Another would be to expose the population to predators, etc. (claim 54). The claims now stress that the "first trait confers resistance to a pesticide…." In the case of claim 54, this trait may also confer "tolerance to predators, viruses, parasites or parasitoids…." Thus, pesticides and agents such as predators (as well as viruses, parasites or parasitoids) can also be used to control the insect population. Both are capable of, and are generally used to, control (i.e. weaken or exert a negative effect on the) insect pest populations.

The present claimed invention sets out to limit or eradicate the first trait, referred to hereinafter solely as the resistance trait (but it of course also refer to tolerance in respect of claim 54). All that the invention requires is that this first (resistance) trait confers an advantage on the pest population. This advantage is the ability to avoid the normal methods of controlling said population.

The key point is that it is counter-intuitive to release more insects into a population and actually promote breeding when one is seeking to control (i.e., kill off) that population. However, what Applicants have found is that the dilution of resistance is best promoted by driving and maintaining the introgression of the sensitive allele into the target population. This is achieved by provision of **substantially homozygous wild type individuals which are sensitive to the pesticide.** In particular, as explained on pages 4 and 5 of the present application, heterozygotes suffer a disadvantage in both the presence and absence of the pesticide. This is

in direct contrast to the lethal gene (engineered) strategy of the cited Alphey reference. Thus, Alphey effectively teaches away from the present invention.

In the presence of the pesticide, the heterozygotes may show some resistance, but are essentially very ill and cannot compete with the resistant homozygotes. Obviously, the wild type individuals die off because they are sensitive to the pesticide.

In the absence the pesticide, the roles are reversed, except that the heterozygotes are still at a disadvantage. The heterozygotes are ill because one of their pathways is thought to be at least partially blocked, and as a result cannot compete on an equal basis with wild type individuals. The resistant homozygotes also cannot compete with the wild type in the absence the pesticide, so also die off. Thus, the promotion of the heterozygote state is beneficial to the controlling population as a whole, as it maintains the presence of the sensitive allele in the population and dilutes the resistant allele.

Thus, due to the counter-intuitive nature of the release (and treatment of pesticide) of further (substantially homozygous wild type individuals) insects into a population one is trying to control, the claimed invention would not have been obvious to one of ordinary skill in the art at the time the invention was made over Alphey, which does nothing to point the skilled person towards the crucial step of releasing substantially homozygous wild type individuals into the target population. The strategy of the present invention offers a surprising solution to the problem of the development of resistance to a pesticide or the like.

In view of the foregoing, Applicant respectfully maintains that the present invention as claimed is not *prima facie* obvious over the cited Alphey reference, and the withdrawal of the rejection is respectfully requested.

Claims 22-26 and 32 have been rejected as allegedly unpatentable over Alphey (WO 01/39599) in view of Buman (US Patent 6,338,040). Applicant respectfully traverses this rejection.

The Alphey reference has been discussed at length above. Applicant respectfully maintains that the Buman reference is of little relevance to the present claimed invention. The

use of refugia is known, as is the use of the Bt toxin. Buman only adds to the art by disclosing a business method focusing on the provision of insurance to assist in making the use of refugia attractive (in the economic sense) to a farmer. The proposed insurance plan of Buman appears to indicate that there is a significant risk of reduced yield in crops planted in refugia. The Buman patent is silent on the release of substantially homozygous wild type individuals who are sensitive to the pesticide with the aim of promoting the heterozygote state to thereby dilute any accumulating resistance and thus prolong the useful lifetime of a pesticide. In the absence of relevant teachings of Buman, the arguments above as to Alphey are applied again here.

In view of the foregoing, Applicants respectfully maintain that the present invention as claimed is not *prima facie* obvious over the cited Alphey and Buman references, and the withdrawal of the rejection is respectfully requested.

Conclusion

In view of the foregoing, it is submitted that this case is in condition for allowance, and passage to issuance is respectfully requested.

If there are any outstanding issues related to patentability, the courtesy of a telephone interview is requested, and the Examiner is invited to call to arrange a mutually convenient time.

This amendment is accompanied by a Petition for Extension of Time (three months) and payment in the amount of $555.00 as required under 37 C.F.R. 1.17(a). It is believed that this amendment does not necessitate the payment of any additional fees under 37 C.F.R. 1.16-1.17. If the amount submitted is incorrect, however, please charge any deficiency or credit any overpayment to Deposit Account No. 07-1969.

Respectfully submitted,

/donnamferber/

Donna M. Ferber, Ph.D.
Reg. No. 33,878

GREENLEE SULLIVAN P.C.
4875 Pearl East Circle, Suite 200
Boulder, CO 80301
Telephone: (303) 499-8080
Facsimile: (303) 499-8089
E-mail: usptomail@greenwin.com
Attorney docket No. 129-05